Jan Bureš, Marcela Kopáčová, Ilona Koupil, Bohumil Seifert, Miluška Škodová Fendrichová, Jana Špirková, Viktor Voříšek, Stanislav Rejchrt, Tomáš Douda, Norbert Král, Ilja Tachecí

Jan Bureš, Marcela Kopáčová, Miluška Škodová Fendrichová, Stanislav Rejchrt, Tomáš Douda, Ilja Tacheci, Second Department of Medicine Gastroenterology, Charles University in Prague, Faculty of Medicine at Hradec Králové, University Teaching Hospital, 50005 Hradec Králové, Czech Republic Ilona Koupil, Centre for Health Equity Studies, Karolinska Institute, Stockholm University, 17177 Stockholm, Sweden Bohumil Seifert, Norbert Král, First Faculty of Medicine, Institute of General Practice, Charles University, 12108 Prague, Czech Republic Jana Špirková, Viktor Voříšek, Institute of Clinical Biochemistry and Diagnostics, Charles University in Prague, Faculty of Medicine at Hradec Králové, University Teaching Hospital, 50005 Hradec Králové, Czech Republic Author contributions: Bureš J, Kopáčová M, Koupil I, Seifert B, Škodová Fendrichová M, Špirková J, Voříšek V, Rejchrt S, Douda T, Král N and Tachečí I contributed equally to this work. Supported by Research Project PRVOUK P37-08 from Faculty of Medicine at Hradec Králové, Charles University in Prague, Czech Republic Correspondence to: Jan Bureš, MD, PhD, Professor, Second Department of Medicine Gastroenterology, Charles University in Prague, Faculty of Medicine at Hradec Králové, University Teaching Hospital, Sokolská 581, 50005 Hradec Králové, Czech Republic, bures@lfhk.cuni.cz Telephone: +420-495-834240 Fax: +420-495-834785 Received: July 3, 2012 Revised: August 13, 2012 Accepted: August 16, 2012 Published online: August 28, 2012

Abstract

AIM: To study possible decrease in prevalence of *Helicobacter pylori* (*H. pylori*) infection in the Czech Republic within a 10-year period.

METHODS: A total of 22 centres entered the study. The catchment areas of these centres covered cities and towns with more than 20 000 inhabitants, smaller towns (< 20 000 inhabitants) with surrounding villages and rural areas, and were spread over the whole country, corresponding well to the geographical distribution of the Czech population. A total of 1 837 subjects (aged 5-98 years) took part in the study, randomly selected out of 38 147 people from the general population. *H. pylori* infection was investigated by means of a 13C-urea breath test. Breath samples in duplicates were analysed using isotope ratio mass spectrometry. The cut-off point was 3.5. Social and demographic characteristics were based on data from self-completed questionnaires.

RESULTS: The overall prevalence of *H. pylori* infection was 23.5% (430/1826), and 4.8% (20/420) in children aged 15 or less. There was no statistically significant difference in prevalence between males (24.3%; 208/857) and females (22.9%, 222/969, P = 0.494). *H. pylori* infection was strongly associated with higher age, among subjects aged 55+ years, prevalence of *H. pylori* infection was 39.8% (252/633, P < 0.001). The highest prevalence of *H. pylori* infection was found among persons aged 55-64 years (43.9%, 97/221) and 75+ years (37.9%, 58/153). Among study subjects aged 15+ years, prevalence of *H. pylori* infection was significantly increased in those with lowest education (odds risk 3.19, 95% CI 1.87-5.47). Compared to never married (14.1%), the prevalence of *H. pylori* infection was statistically significantly higher among married (35.4%, 246/694, P < 0.001), divorced (36.8%, 49/133, P < 0.001) and widowed study subjects (40.2%, 45/112, P < 0.001), both in minimally and fully adjusted analysis. There was no significant difference in the prevalence of *H. pylori* infection between married and widowed subjects (35.4%, 246/694 vs 40.2%, 45/112, P = 0.389). There was little variation in smoking prevalence across categories of smoking and there was no evidence of an increased risk of *H. pylori* infection among current or past smokers in our data (odds risk 1.04 with 95% CI 0.78-1.40 for current smokers; odds ratio 0.83 with 95% CI 0.60-1.16 for former smokers). The current prevalence of *H. pylori* infection was statistically significantly higher among current or past smokers in our data (odds risk 1.04 with 95% CI 0.78-1.40 for current smokers; odds ratio 0.83 with 95% CI 0.60-1.16 for former smokers).
in 2011 was significantly lower compared to the prevalence reported from identical geographical areas in 2001 (23.5% vs 41.7%, $P < 0.001$).

CONCLUSION: The overall prevalence of *H. pylori* infection in the general population has fallen substantially in the Czech Republic over the past 10 years.

© 2012 Baishideng. All rights reserved.

Key words: Epidemiology; *Helicobacter pylori*; Czech Republic; 13C-urea breath test; Decline of prevalence

Peer reviewer: Fabio Pace, Professor, Division of Gastroenterology, L. Sacco University Hospital, University of Milan, Via G.B. Grassi, 74, 20157 Milano, Italy


INTRODUCTION

*Helicobacter pylori* (*H. pylori*) infection is still the most common human infection worldwide. It is estimated that 50%-80% of the population is infected[4-8]. The prevalence in developed countries of Europe is 10%-30% (with an increase of 1%-3% for each age decade). Up to 95% of the adult population is infected in developing countries[4-8].

Our group accomplished a large multi-centre epidemiologic study on the prevalence of *H. pylori* and dyspepsia in the Czech Republic, a Central European country, in 2001[9-11]. The Project was executed on a total of 2509 persons aged 5-100 years, randomly selected out of 30 012 subjects from the general population. *H. pylori* infection was investigated by means of 13C-urea breath test. The overall prevalence of *H. pylori* was 41.7% in 2001[9]. Meanwhile, several concerns have been raised about the possible decrease of *H. pylori* prevalence in developed countries. The aim of our current multi-centre prospective study was to evaluate the prevalence of *H. pylori* infection in the Czech Republic using the same methods in a representative sample of general unselected population from the same geographical areas 10 years later.

MATERIALS AND METHODS

Study population

A total of 22 centres entered the study. They included 15 centres of general practitioners for adults and 7 for children and adolescents. These centres covered cities and towns with more than 20 000 inhabitants (10 centres), smaller towns (≤ 20 000 inhabitants) with surrounding villages (9 centres) and rural areas (3 centres), and were spread over the whole country, corresponding well to the geographical distribution of the Czech population. A total of 1837 subjects (aged 5-98 years) took part in the study, randomly selected out of 38 147 registered males and females in this age range.

Urea breath test

Urea breath tests were performed in the morning after overnight fasting by means of 13C-urea breath test[12]. Citric acid solution (3 g dissolved in 150 mL of still water) was given initially as a test drink. Five min later two baseline exhaled breath samples were collected into 20-mL vacutainers using a straw. Thereafter all persons ingested 75 mg 13C-urea (*Helicobacter* Test INFAI, INFAI GmbH, Köln, Germany) dissolved in 50 mL of still water with 1 g citric acid (at time 0). Breath samples were collected in duplicates using a straw into 20-mL vacutainers after 30 min. Tubes with breath samples were sent to a single analytical centre by post and measured within a one-week period. Breath samples in duplicates were analysed using isotope ratio mass spectrometry (AP 2003, Analytical Precision Products, Cambridge, United Kingdom). The cut-off point was 3.5. Results of 13C-urea breath test for *H. pylori* status were obtained for 99.4% (1826/1837) of subjects.

Questionnaires

Data were collected by self-completed questionnaires distributed to adults and parents of children aged 5-15 years. The questionnaire included information on place of residence in childhood, mother’s and father’s education, access to running warm water in childhood, crowding in childhood and number of siblings. Information on the study subjects’ current place of residence, education, marital status, self-reported socio-economic group and smoking habits was also collected in the questionnaire and was used in the analysis of determinants of *H. pylori* positivity in subjects aged above 15 years.

Ethical approval

The study was approved by the University Ethics Committee. All participants received detailed written information about the Project in advance and signed written consent (parents on behalf of their children). For all data obtained, all personal identification information was deleted in compliance with the laws for the protection of confidentiality of the Czech Republic.

Statistical analysis

The data was analysed using STATA statistical software (StataCorp. 2011. Stata Statistical Software: Release 12, College Station, TX). Education was analysed in six categories (university, secondary, vocational higher and lower, elementary and students) and marital status in five categories (single, first time married, re-married, divorced and widowed). In the analysis, we used three categories.
of smoking (never smoker, past smoker and current smoker). Proportions were compared using Chi-square test and the relative risk of *H. pylori* infection was studied in logistic regression with adjustment for age, gender and other social variables. Multivariable analyses were restricted to subjects with non-missing data on the variables studied.

**RESULTS**

The overall prevalence of *H. pylori* infection was 23.5% (430/1826), and 4.8% (20/420) in children aged 15 or less. There was no statistically significant difference in prevalence between males (24.3%, 208/857) and females (22.9%, 222/969, P = 0.494). *H. pylori* infection was strongly associated with higher age (Table 1).

Among study subjects aged above 15 years, prevalence of *H. pylori* infection was significantly increased in those with lowest education (Table 2). Compared to never married, the prevalence of *H. pylori* infection was statistically significantly higher among married and divorced study subjects, both in minimally and fully adjusted analyses (Table 2). There was little variation in smoking prevalence across categories of smoking and there was no evidence of an increased risk of *H. pylori* infection among current or past smokers in our data (Table 2).

The current prevalence of *H. pylori* in 2011 was significantly lower compared to the prevalence reported from identical geographical areas in 2001 (23.5% vs 41.7%, P < 0.001).

**DISCUSSION**

Our multi-centre prospective study proved that the current prevalence of *H. pylori* in 2011 is significantly lower compared to the prevalence of identical geographical areas in 2001. Both our studies were based on a representative sample of the general population, covering large and small urban population as well as rural areas and using 13C-urea breath test as a gold standard for *H. pylori* diagnostics. Thus our results are reliable and trustworthy. The decline of *H. pylori* was found not only in overall prevalence but also in particular age decades. Explanation of this phenomenon is not easy and unequivocal. Although there are no strictly unimpeachable epidemiologic data available, the decrease of *H. pylori* prevalence probably already started in the Czech Republic in the late 1990's. It could be explained mostly by the relatively favourable and improving socio-economic conditions and standards of living together with falling fertility rates. In the same period, the age-standardised death rate from stomach cancer in the Czech Republic fell from 17.3/100 000 (in 1992) to 11.9/100 000 (2001) followed by further current decline to 8.7/100 000 (in 2010) [19,20]. Two large Czech seroprevalence studies found decreased *H. pylori* prevalence in the mid 2000's among subjects screened for thyroid disease [21,22] and in patients with peptic ulcer disease, functional dyspepsia and gastro-oesophageal reflux disease [23-25]. Decrease in the prevalence of *H. pylori* infection was also reported in other former communist countries such as Estonia (in children from 42% in 1992 and 41% in 2002) [26], Slovakia (in adults from 52% in 1992 and 41% in 2002 to 35% in 2007) [27,28] and Russia (in children from 44% in 1995 to 13% in 2005) [29]. This decline in *H. pylori* prevalence was explained by the profound socio-economic changes after the fall of communist regimes.

However, significant decrease of the prevalence of *H. pylori* infection was also found in stable developed European countries like the Netherlands [30-32], Finland [33,34], the United Kingdom [35,36], Germany [37], Norway [38] and Denmark [29]. This decrease could not be explained only by the birth-cohort phenomenon either. In developed countries, spontaneous subsequent clearance of *H. pylori* infection seems to be common [39]. In Finland, decrease of prevalence of *H. pylori* infection is believed to be due to the “screen and treat” project [41,42]. The main explanation for the decrease in *H. pylori* prevalence cannot merely be wide use of antibiotics for various indications.

---

**Table 1**: Prevalence of *Helicobacter pylori* by age and gender in a representative sample of Czech population n (%)  

<table>
<thead>
<tr>
<th>Age (yr)</th>
<th>Males</th>
<th>Females</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-14</td>
<td>188 (4.8)</td>
<td>197 (5.1)</td>
<td>385 (4.9)</td>
</tr>
<tr>
<td>15-24</td>
<td>124 (10.5)</td>
<td>151 (7.9)</td>
<td>275 (9.1)</td>
</tr>
<tr>
<td>25-34</td>
<td>97 (16.5)</td>
<td>107 (13.1)</td>
<td>204 (14.7)</td>
</tr>
<tr>
<td>35-44</td>
<td>84 (30.9)</td>
<td>79 (19.0)</td>
<td>163 (25.1)</td>
</tr>
<tr>
<td>45-54</td>
<td>73 (42.5)</td>
<td>93 (34.4)</td>
<td>166 (37.9)</td>
</tr>
<tr>
<td>55-64</td>
<td>94 (42.5)</td>
<td>127 (44.9)</td>
<td>221 (43.9)</td>
</tr>
<tr>
<td>65-74</td>
<td>122 (38.5)</td>
<td>137 (36.5)</td>
<td>259 (37.4)</td>
</tr>
<tr>
<td>≥ 75</td>
<td>75 (34.7)</td>
<td>78 (41.0)</td>
<td>153 (37.9)</td>
</tr>
</tbody>
</table>

---

**Table 2**: Prevalence of *Helicobacter pylori* by social characteristics and smoking in a representative sample of Czech population  

<table>
<thead>
<tr>
<th>Marital status</th>
<th>n</th>
<th>H. pylori (%) OR1 (95% CI) OR2 (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Never married</td>
<td>488</td>
<td>14.1</td>
</tr>
<tr>
<td>First time married</td>
<td>566</td>
<td>34.8</td>
</tr>
<tr>
<td>Re-married</td>
<td>128</td>
<td>38.3</td>
</tr>
<tr>
<td>Divorced</td>
<td>133</td>
<td>36.8</td>
</tr>
<tr>
<td>Widowed</td>
<td>112</td>
<td>40.2</td>
</tr>
</tbody>
</table>

---

Czech population aged above 15 years and examined in 2011 (n = 1427).  
1Adjusted for age and gender; 2Adjusted for age, gender and mutually adjusted for other variables. OR: Odds ratio; *H. pylori*: *Helicobacter pylori*. 

---

Bureš J et al. Epidemiology of *H. pylori* in the Czech Republic.
The prevalence of *H. pylori* infection is significantly lower in patients with inflammatory bowel disease but not in those with chronic obstructive pulmonary disease (despite extensive antibiotic use). There was no difference in *H. pylori* prevalence in Crohn’s disease with or without previous treatment with sulfasalazine or antibiotics.

In our previous study, we did not find a birth-cohort phenomenon of *H. pylori* infection after the Second World War, in contrast to developed countries. This could be explained by the great migration of population in former Czechoslovakia after the Second World War, forced unnatural collectivisation (in fact expropriation) of agriculture, equalisation of society and mostly low socio-economic status under the communist government. den Hoed et al. found a new birth-cohort phenomenon of *H. pylori* infection in the Netherlands. They observed a decline in *H. pylori* prevalence in 6- to 8-year-old Dutch children from 19% in 1978 to 9% in 1993. The further prevalence of *H. pylori* in childhood has remained stable in the Netherlands from 1993 to 2005, suggesting a stabilisation of the previously decreasing trend in subsequent birth cohorts. This finding may reflect stabilisation in determinants such as family size, housing, and hygienic conditions (or offset by day care).

Several interesting data came from other studies outside Europe. Decreased prevalence of *H. pylori* was also found for instance in the United States, China, Japan, South Korea and Singapore. After fifteen years, the prevalence of *H. pylori* infection among both children and adults in China remained significantly higher in areas with a high incidence of gastric cancer compared with that in areas with a low incidence of gastric cancer. *H. pylori* infection rates have decreased in the general Chinese population during recent years.

Poor standard of living, low socio-economic status, overcrowded families, low education of parents and smoking (in adults) are still major risk factors of *H. pylori* infection. Acquisition, chronic infection and possible spontaneous clearance of *H. pylori* are influenced by several other factors such as ethnicity and genetic factors. Extensive broad use of antibiotics for different indications might be less important.

It is necessary to revive the so-called hygiene hypothesis. It was suggested that with the higher hygiene standards in developed countries, people (especially raising children) are less exposed to helminths and this fact modulates development of the immune system (Th1/Th2 shift of CD4+ T-lymphocytes) and thereby increases the risk of several diseases like inflammatory bowel disease, bronchial asthma, food allergy and many others. The high prevalence of *H. pylori* and low rate of gastric cancer in Africa and some parts of Asia were called the “African or Asian (Indian) Enigma” and explained merely by the high prevalence of helminth infections. Subsequent prospective studies found that no such dissociation existed. Nowadays the “African Enigma” is considered to be a myth. Nevertheless, hygiene theories should be considered in explanation of the gradual decline of *H. pylori* infection. Blaser and his group pointed out an inverse association between *H. pylori* infection and bronchial asthma, even though not confirmed by some others. Sonnenberg et al. found low prevalence of *H. pylori* infection in inflammatory bowel disease.

Sýkora et al. published an excellent study on *H. pylori* among children in the Western Bohemian region (based on *H. pylori* stool antigen testing). The overall prevalence was 7.1% among 1545 children (aged 0-15 years; in the period 2003-2005). Breast-feeding was an important protective factor, *H. pylori* was found in 12.4% children that were not breast-fed. The prevalence of *H. pylori* was 80.8% among subjects living in children’s homes in this study.

Smoking is another independent risk factor for *H. pylori* infection in adults. The lower number of current smokers in Europe might also influence the decline of *H. pylori* infection. In our previous study in 2001, smoking habits were strongly related to risk of *H. pylori* positivity in adults, men and women with lowest education and heavy smokers being at the highest risk of *H. pylori* infection. Surprisingly, there was no evidence of an increased risk of *H. pylori* infection among current or past smokers in our present study. It is necessary to mention another interesting phenomenon: the decreased prevalence of *H. pylori* represents a prominent decline of CagA positive *H. pylori* strains. Explanation for this finding still remains unclear.

However, several studies recently showed that the prevalence of *H. pylori* is also declining among children in developing countries like Uganda, Brazil and the Middle East region despite persisting poor hygiene, standard of living and low socio-economic conditions.

On top of all those aspects mentioned above, it is necessary to admit that the reasons for decline of *H. pylori* infection have not been fully clarified yet. It is necessary to also consider the fundamental determinants of “modern times” that could cause gradual disappearance of *H. pylori* from the human microbiome.

In summary, the overall prevalence of *H. pylori* infection in the general population has fallen substantially in the Czech Republic over the past 10 years. This decrease can be explained mostly by the relatively favourable and improving socio-economic status and high standard of living conditions. However, it is necessary to also consider that both environmental factors and the human host create an unfavourable milieu responsible for the decline of *H. pylori* infection.

ACKNOWLEDGMENTS

Our sincerest thanks go to all general practitioners and their staff. They performed some really great work in their respective centres. Project participants: Šárka Bílková, MD (Slaný), Pavel Brejník, MD (Kladno), Otto Herber, MD (Veltrusy), Petr Herle, MD (Praha 4), Otakar Ach-Hübner, MD, (Brno), Eva Charvatová, MD (Praha 4), Karel Janík, MD (Horní Bečva), Olga Kobesová MD (Praha 10), Tomáš Koudelka, MD (Počátky), Gréta Koudelková, MD (Žatec), Milada Kratochvílová, MD

---

WJG | www.wjgnet.com
Bureš J et al. Epidemiology of H. pylori in the Czech Republic

(Brno), Miloš Ponižil, MD (Hrušovany nad Jevišovkou), Assoc. Professor Bohumil Seifert, MD, Ph.D. (Praha 8), Helena Vesešá, MD (Chýně), Norbert Král, MD (Praha 2), Jana Vojtíšková, MD (Praha 2), Ruth Adamová, MD (Čáslav), Romana Balatková, MD (Most), Irena Bumbová, MD (Kamenné Žehrovice), Jana Ponižilová, MD (Hrušovany nad Jevišovkou), Miroslava Šircová, MD (Slaný), Jarmila Seifertová, MD (Kladno) and Věra Ševčíková, MD (Praha 2).

REFERENCES
24. Rehmberg-Laiho L, Salomaa A, Rautelin H, Koskela P, Sarra N, Kosunen TU. Accelerated decline in Helicobacter pylori seroprevalence rate during the screen and treat project in Vammala, Finland, as demonstrated in 29- to 45-year-old pregnant women. APMIS 2004; 112: 34-38
not resulted in fewer hospital admissions for peptic ulcer disease-related complications. *Aliment Pharmacol Ther* 2007; 25: 1423-1427


60 Manuel D, Cutler A, Goldstein J, Fennerty MB, Brown K. Decreasing prevalence combined with increasing eradication of Helicobacter pylori infection in the United States has...
licobacter pylori infection: cross sectional study. BMJ 1997; 315: 1489-1492


64 Kawakami E, Machado RS, Ogata SK, Langner M. Decrease in prevalence of Helicobacter pylori infection during a 10-year period in Brazilian children. Arq Gastroenterol 2008; 45: 147-151


71 Blaser MJ. Helicobacter pylori and esophageal disease: wake-up call? Gastroenterology 2010; 139: 1819-1822

72 Blaser MJ. Heterogeneity of Helicobacter pylori. Eur J Gastroenterol Hepatol 2012; 9 Suppl 1: S3-6; discussion S6-7

S- Editor Gou SX L- Editor Xiong L